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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,160	04/12/2005	Boris Y Shekunov	FER-14857.001.001	4722
7609 7590 07/26/2007 RANKIN, HILL, PORTER & CLARK, LLP 925 EUCLID AVENUE, SUITE 700 CLEVELAND, OH 44115-1405			EXAMINER EBRAHIM, NABILA G	
			ART UNIT 1618	PAPER NUMBER
			MAIL DATE 07/26/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/531,160	Applicant(s) SHEKUNOV ET AL.	
	Examiner Nabila G. Ebrahim	Art Unit 1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 May 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7, 15-21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7 and 15-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1618

DETAILED ACTION

Receipt of Applicant's remarks and amendments to the claims dated 5/7/07 is acknowledged.

Status of Claims

Claims 1-7, and 15-21 are pending in the application and under current examination.

Claims 8-14 were cancelled.

Status of Office Action: Final

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 1-7, and 15-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Subramaniam et al. US 5,874,029 (hereinafter "Subramaniam") in view of Henriksen et al. US 6974593 (hereinafter "Henriksen").

Subramaniam teaches a method and an apparatus useful for the production of microparticles and nanoparticles.

The steps are:

Adding a solvent to a solute forming a mixture.

Art Unit: 1618

Adding the mixture to the SCF (which is a non-solvent)

Getting the particles out of the solute. (see abstract)

The invention can be used in the pharmaceutical, food, chemical, electronics, catalyst, polymer, pesticide, explosives, and coating industries, all of which have a need for small-diameter particles (abstract). The method comprises solutes such as drug, polymer, and/or excipient materials are solubilized. The supercritical antisolvent used is supercritical carbon dioxide (col. 6, lines 27, and 28), also a trifluoromethane is used (claim 12), which is encompassed by fluorocarbons recited in the current application, and poly-lactide glycolide copolymers (claim 22).

Subramaniam discloses the limitation recited in claim 8 regarding functional group of portion that is SCF-philic and SCF-phobic since the current specification discloses in paragraph [0015 and 0027] teaches that any compounds that comprise both SCF-philic groups, which make the compound soluble in SCF, and SCF-phobic groups, which have an affinity or attraction to the nuclei of the material(s) formed during the precipitation step, can be employed as growth retardant compounds. Examples of growth retardant compounds for use with supercritical carbon dioxide ($SC-CO_2$) include fluorocarbons. Accordingly, Subramaniam discloses a trifluoromethane, which is encompassed by the group of fluorocarbons. In addition the limitations recited in independent claim 15 of the instant application regarding expanding the SCF solution across a pressure drop below the critical pressure of the SCF whereby the SCF decompresses and causes supersaturation and nucleation of particles comprising the solute material, said particles having a smaller size and a reduced amount of agglomeration than if no growth retardant compound was present. Subramaniam discloses that following the drying period, the pressure is decreased to atmospheric level (col. 9, lines 11-24). Furthermore Subramaniam teaches that accurate pressure control is essential in the highly compressible near-critical region. Pressure fluctuations in this region have a strong effect on the level of expansion of the organic solution and thus on the level of supersaturation and nucleation (col. 9, 25-29, col. 5, line 40, 41 and example 1).

Art Unit: 1618

Subramaniam is deficient in disclosing growth retardant as sugar acetate, fluorocarbons or block polymers.

Henriksen teaches particles of water insoluble biologically active compounds, particularly water-insoluble drugs, with an average size of 100 nm to about 300 nm, are prepared by dissolving the compound in a solution then spraying the solution into compressed gas, liquid or supercritical fluid in the presence of appropriate surface modifiers (abstract). Henriksen teaches a method that comprises (1) precipitating a compound by rapid expansion from a supercritical solution (Rapid expansion from supercritical solution) in which the compound is dissolved, or (2) precipitating a compound by spraying a solution, in which the compound is soluble, into compressed gas, liquid or supercritical fluid which is miscible with the solution but is antisolvent for the compound. In this manner precipitation with a compressed fluid antisolvent (Compressed fluid antisolvent) is achieved. Optionally, the process combines or integrates a phospholipid in water or other suitable surface modifiers such as surfactants, as may be required, into the processes. The surfactant is chosen to be active at the compound-water interface, but is not chosen to be active at the carbon dioxide-organic solvent or carbon dioxide compound interface when carbon dioxide is used as the supercritical solution (col. 2, lines 30+). Specifically, examples of suitable second surface modifiers include one or combination of the following: block copolymers of ethylene oxide and propylene oxide and a tetrafunctional block copolymer derived from sequential addition of ethylene oxide and propylene oxide (col. 3, lines 37+).

Though Henriksen uses these compounds as surfactants and does not disclose literally "growth retardants", it is noted that provisional application 60475547 which Applicant claims priority to discloses the surfactant as alternative term for growth retardant (see specification pages 4, and 5).

Accordingly, it would have been obvious to one of ordinary skills in the art to use surfactants as polyethylene and polypropylene oxides to improve the outcome of the particles produced by micronization and nanonization of a solution containing insoluble active agent and organic solvent which is sprayed into compressed antisolvent because Henriksen discloses that to date of his invention, it has not been possible to make submicron particles by the compressed

Art Unit: 1618

fluid antisolvent process without particle aggregation or flocculation. The objective is to overcome this limitation with the use of surface modifiers, also termed surfactant stabilizers (col. 5, lines 57+). The expected results would be a method of producing particles using a supercritical fluid which has less tendency to aggregate.

It is noted that the filing date of Henriksen is June 9, 2003 while the instant application claims benefit of 60/475,547 06/03/2003. However provisional 60/475,547 does not claim the copolymers recited in the instant claims. Provisional application 60/475,547 discloses polymers in the first paragraph only as follows:

The current invention relates to a method of the formation of solid compositions using supercritical fluids. The solid compositions either consists of pure particles of a material/materials or particles of a coating material/materials (biodegradable polymer or lipid) having a pharmaceutical product encapsulated or adsorbed within its matrix. The current invention is highly suited for precipitation of non-agglomerated nanoparticles of pharmaceuticals or a blend of pharmaceuticals for drug delivery.

Accordingly, Henriksen is properly used in the rejection.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Art Unit: 1618

2. Claims 1-7, and 15-21 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 9-13, 15, and 16 of copending Application No. 10/534,665.

Claims of application '665 recite the steps of mixing a solute in a solvent, contacting the solution with a liquefied gas (carbon dioxide), expanding the mixture to form droplets, and extracting the solvent to get the particles. The process includes sugars, or stabilizers, and the particles size range recited is within 0.05 to one micron (the range recited in the current application is less than 10 micron and more than 300 nm which encompass the range recited in '665). Thus the instant claims are fully encompassed by the claims of the copending application.

This is a provisional obviousness-type double patenting rejection.

3. Claims 1-21 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6, 9-12, and 14-15 of copending Application No. 10/789422.

Application '422 recites a method of producing particles in which the steps are providing a supercritical fluid (carbon dioxide), two solvents, one is soluble in the SCF, the other is substantially insoluble in the SCF and partially soluble in or miscible with the first solvent and a solute (active agent) which is soluble in the first solvent and is substantially insoluble in the second solvent and the supercritical fluid. Then contacting the two solvents with solute, then contacting the solution with SCF then precipitate the solute to extract the particles from the solvents. The process may include an excipient and the targeted particle size is between 10 micron and 10 nm (the range overlaps with the instant application disclosure). Thus the instant claims are fully encompassed by the claims of the copending application.

This is a provisional obviousness-type double patenting rejection.

Response to Arguments

4. Applicant's arguments filed 5/7/07 have been fully considered but they are not persuasive.

Applicant argues that:

Art Unit: 1618

- Subramaniam does not ever disclose, teach or suggest that growth retardant compound should be mixed into the solution before the solution and the supercritical fluid are contacted together.

To respond: Subramaniam's method comprises supercritical antisolvent which is supercritical carbon dioxide, trifluoromethane (claim 12), which is encompassed by fluorocarbons recited in the current application.

- The Examiner contends that because applicants claim (e.g., in claim 3) that the growth retardant compound can be selected from "fluorocarbons", and because Subramaniam et al. mentions trifluoromethane ("CHF3"), Subramaniam et al. teaches the invention as claimed in claim 1. This is clearly incorrect. Subramaniam et al. mentions trifluoromethane ("CHF3") once, and only in the context of trifluoromethane ("CHF3") being suitable for use as an antisolvent (i.e., the material into which the solution is atomized, and not a constituent of the solution).

To respond: this was not found persuasive because, if the Examiner found that trifluoromethane was disclosed by Subramaniam as an ingredient of the solution and as recited in claim 1, the claim would have been rejected under 35 USC §102. On the contrary, Examiner added Henriksen -as a secondary reference- who teaches particles of water insoluble drugs, with an average size of 100 nm to about 300 nm, which are prepared by dissolving the compound in a solution then spraying the solution into compressed gas, liquid or supercritical fluid in the presence of appropriate surface modifiers (abstract). note that the Examiner showed in the office action that Henriksen uses these compounds as surfactants and does not disclose literally "growth retardants", it is noted that provisional application 60475547 which Applicant claims priority to discloses the surfactant as alternative term for growth retardant (see specification pages 4, and 5).

- Applicant contends that Henriksen did not have the surfactant in the solution.

To respond: it is noted that Henriksen teaches that the surfactant is chosen to be active at the compound-water interface, but is not chosen to be active at the carbon dioxide-organic solvent or carbon dioxide compound interface when carbon dioxide is used as the supercritical solution (col. 2, lines 30+). Since the instant claims do not recite that the solution should be mixed with the

Art Unit: 1618

growth retardant for a period before spraying, then it is within the scope of the instant application to use the surfactant (growth retardant) any time before spraying.

- There is clearly no reason one skilled in the art would combine the teachings of Henriksen et al. with Subramaniam et al. Both accomplish the same goal (reduced particle size), but do so using different means.

To respond: because the two references are dealing with reduced particle size of insoluble drug or compound, these are analogous with the instant claims which is within the same scope. In addition, the motivation for combining is clear since it was obvious to one of ordinary skills in the art to use surfactants as polyethylene and polypropylene oxides to improve the outcome of the particles produced by micronization and nanonization of a solution containing insoluble active agent and organic solvent which is sprayed into compressed antisolvent because Henriksen discloses that to date of his invention, it has not been possible to make submicron particles by the compressed fluid antisolvent process without particle aggregation or flocculation. The objective is to overcome this limitation with the use of surface modifiers, also termed surfactant stabilizers (col. 5, lines 57+). The expected results would be a method of producing particles using a supercritical fluid, which has less tendency to aggregate.

- Subramaniam et al. does not teach a process whereby a supercritical fluid is rapidly expanded across a pressure drop as claimed in claim 15. Henriksen et al. does not disclose the same invention as claimed in claim 15 and its teachings cannot be combined with Subramaniam et al.

To respond: Henriksen teaches the step of expanding SCF solution containing comprising a water insoluble solute across a pressure drop. Once the same step in a similar method is known it would be obvious to one of ordinary skill in the art to determine the best compounds to use in the method to reach the best results.

Conclusion

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

Art Unit: 1618

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nabila G. Ebrahim whose telephone number is 571-272-8151. The examiner can normally be reached on 8:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nabila Ebrahim
7/21/07


MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER